AD-A151 250 RESEARCH IN ENERGETIC COMPOUNDS(U) FLUOROCHEM INC AZUSA CA T G ARCHIBALD ET AL. JAN 85 2-7-ONR N00014-78-C-0147 1/1

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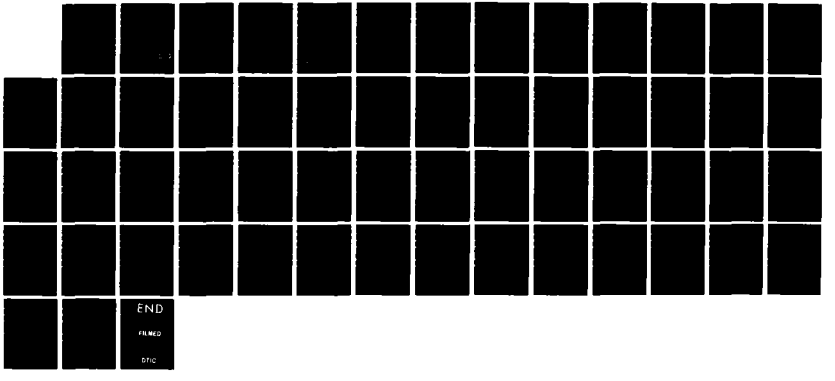

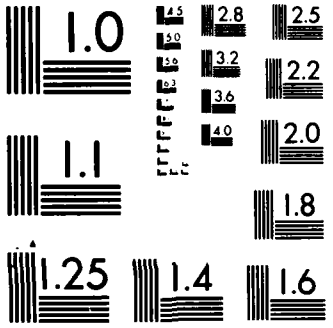

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REPORT No. ONR-2-7 (Interim)

PERIOD COVERED: 1 January 1984 through 31 December 1984

RESEARCH IN ENERGETIC COMPOUNDS

A Report on Work Sponsored by the
OFFICE OF NAVAL RESEARCH

Contract N00014-78-C-0147
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January 1985

FLUOROCHEM, INC.

680 South Ayon Avenue
Azusa, California 91702

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By

T. G. Archibald and K. Baum

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REPORT DOCUMENTATION PAGE	READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER: ONR-2-7	2. GOVT ACCESSION NO. AD-A151250 / 3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Research in Energetic Compounds	5. TYPE OF REPORT & PERIOD COVERED Interim Summary 1 Jan 1984 - 31 Dec 1984
	6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Thomas G. Archibald and Kurt Baum	8. CONTRACT OR GRANT NUMBER(s) N00014-78-C-0147
9. PERFORMING ORGANIZATION NAME AND ADDRESS Fluorochem, Inc. 680 S. Ayon Ave. Azusa, CA 91702	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS NR 659-796/11-18-83
11. CONTROLLING OFFICE NAME AND ADDRESS Department of the Navy Office of Naval Research, Code 432 Arlington, VA 22217	12. REPORT DATE January 1985
	13. NUMBER OF PAGES 54
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)	15. SECURITY CLASS. (of this report) Unclassified
	15a. DECLASSIFICATION DOWNGRADING SCHEDULE

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18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Nitroazetidines
Nitroheterocycles
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Nuclear magnetic resonance spectra
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Chromatography

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

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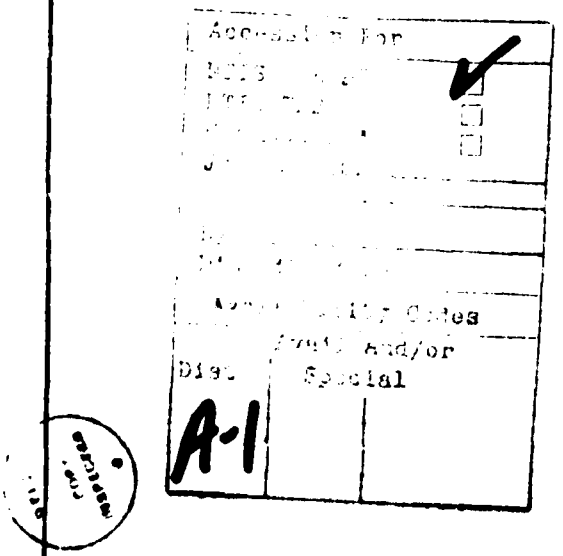
4,4,8,8-Tetranitrobicylo[3 3.0]-2,6-dioxaoctane was synthesized from 4,8-di-p-tosylatobicyclo[3.3.0]-2,6-dioxaoctane. The diazide, obtained by displacement, was reduced to the diamine. Oxidation with MCPBA gave the dinitro compound, and oxidative nitration gave the tetranitro derivative. Work was initiated on the synthesis of nitro-substituted biazetidines and fused tetrahydropyran derivatives. Reactions of mannitol hexatosylate and of 1,6-dibromo-2,5-dichloro-3,4-dimethanesulfonatohexane with t-butylamine resulted in elimination rather than substitution. 3,4-Di(methanesulfonato)hexa-1,5-diene diepoxide was synthesized, but its reaction with amines did not give the desired bicyclic amines. Reported reactions of amines with formaldehyde to give 1,3-dialkyl-1,3-diazetidines could not be duplicated. Reactions of 1,3-dichloro-2-nitro-2-azapropane with amines did not give diazetidines. Work on the synthesis of 1,3,3-trinitroazetidine is summarized as a manuscript.



CONTENTS

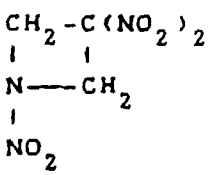
I. INTRODUCTION

This report summarizes the research under Contract N00014-78-C-147 during the period 1 January 1984 through 31 December 1984. The objective of this work is the synthesis of new high density, high energy compounds for explosives applications. In the preceding report period[1], emphasis was placed on the synthesis of 1,3,3-trinitroazetidine, and during the present period some additional work was carried out to improve the synthesis process. This area is summarized in manuscript form as Appendix A. Extension of this work led to research on polynitro compounds with coupled four-membered rings, and their isomers with fused five-membered rings.

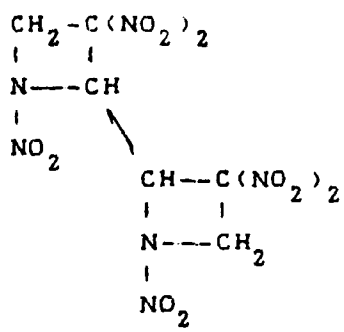
II. HETEROCYCLIC BICYCLO[3.3.0]OCTANES

A. DISCUSSION

As an extension of the 1,3,3-trinitroazetidine work[2], the analogous bis-azetidine structure, which gives higher calculated density and performance properties, was selected as a target. Examples of this ring system, even without subsituents, have not been reported.

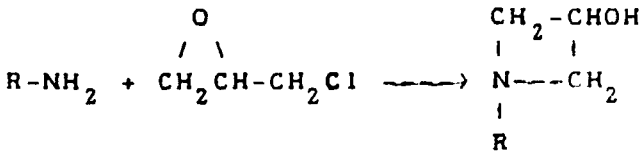


Density 1.82

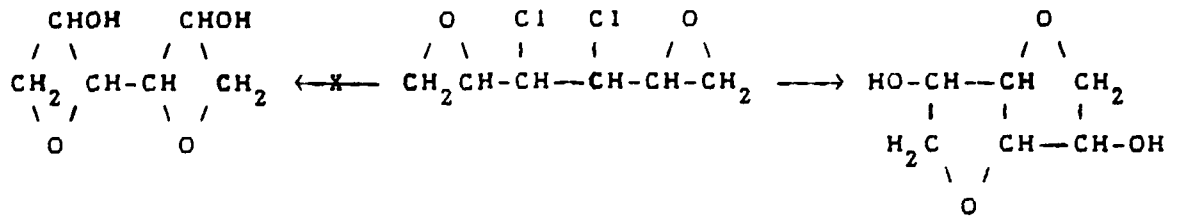


Calculated density 1.88

Conceptually, since azetidines[3] are produced from reactions of amines with epichlorohydrin, suitable starting materials should be accessible through dimers of epichlorohydrins.



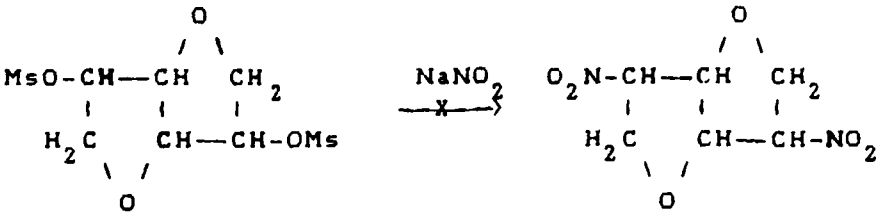
It has been reported, however, that the hydrolysis of dihalo hexane diepoxides yields the isomeric bicyclo[3.3.0]-2,6-dioxaoctanes[4] instead of dimeric oxetanes.



The analogous bicyclic nitrogen ring system is also of interest, inasmuch as its density should be close to that of the dimeric azetidine. Since this nitrogen system, with a bicyclo[3.3.0]-2,6-diazaoctane backbone, is also virtually unknown, the more readily accessible bicyclo[3.3.0]-2,6-dioxaoctanes were used as model compounds.

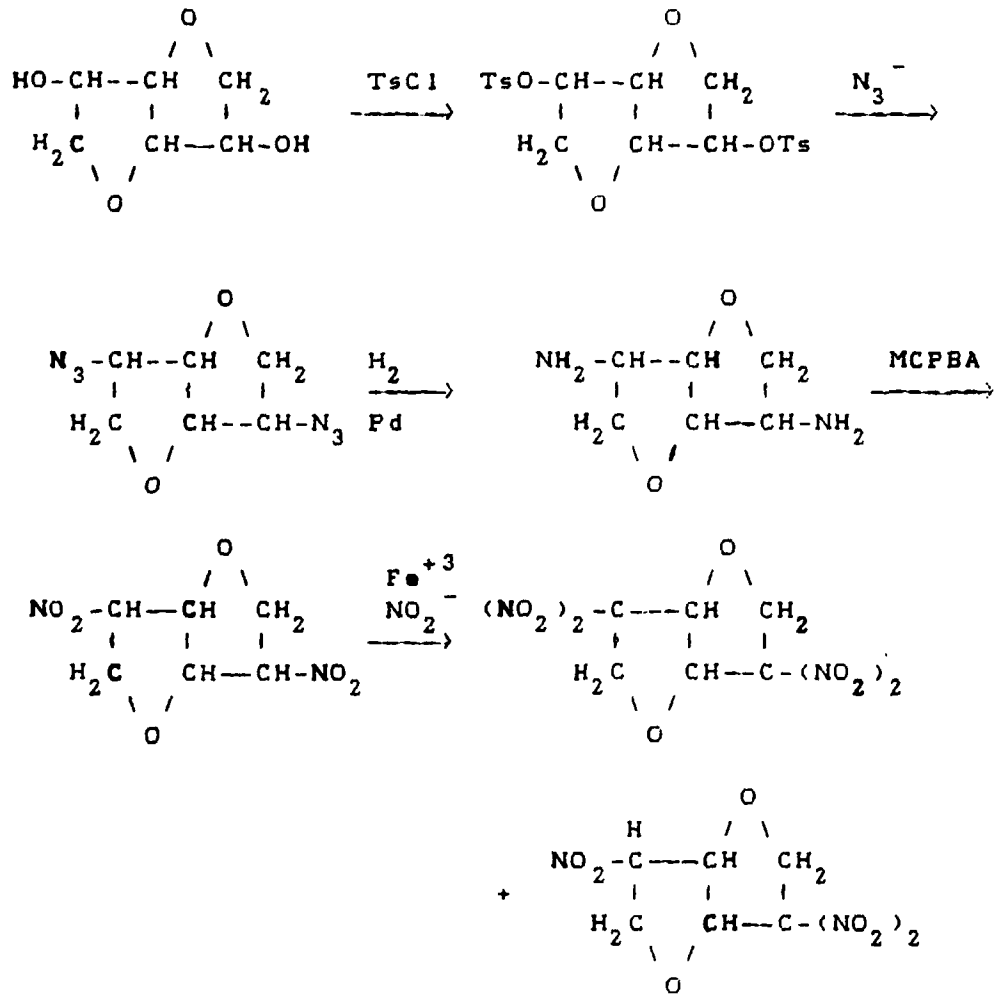
Hexitols, such as D-mannitol, give high yields of 4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane[4] by dehydration with concentrated hydrochloric acid. Three isomers are possible, and each is produced from the hexitol with the proper stereochemistry. Thus, D-mannitol gives endo,-endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane; D- sorbitol, the endo,exo derivative; and D-iditol, the exo,exo derivative. The dihydroxy derivatives were converted to the corresponding ditosylates or dimethanesulfonates. It has been reported[5] that because of steric reasons, only

the endo,endo- ditosylates or dimethansulfonates can undergo displacement reactions, and these reactions take place with great difficulty. We were unable to produce nitro derivatives of bicyclo[3.3.0]-2,6-dioxaoctanes by direct displacement with sodium nitrite.



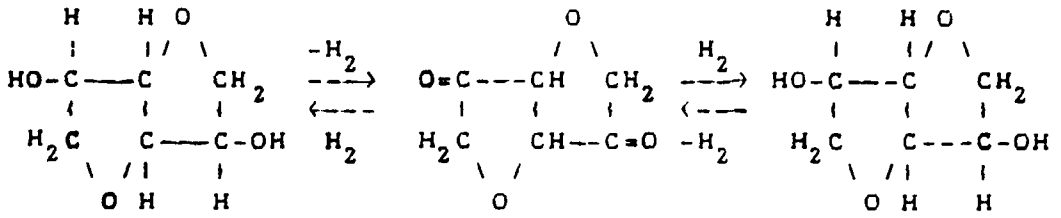
We encountered similar problems previously in the synthesis of 2,2-dinitrooxetane[2], and found that azide ion could be used satisfactorily as a nucleophile. The same reactions were therefore applied to the present synthesis.

Endo,endo-4,8-di-p-tosylatobicyclo[3.3.0]-2,6-dioxaoctane[6] was converted to the exo,exo-diazide in 50% yield by reaction with sodium azide in diethylene glycol at 130°C. Reduction of this diazide with hydrogen over palladium on carbon gave an 88% yield of exo,exo-4,8-diaminobicyclo[3.3.0]-2,6-dioxaoctane. This diamine was previously made in low yield from the direct reaction of the ditosylate with ammonia[7]. The diamine was oxidized with m-chloroperbenzoic acid in dichloroethane to give exo,exo-4,8-dinitrobicyclo[3.3.0]-2,6-dioxaoctane in 32% yield. The dinitro derivative was then converted by the potassium ferrocyanide - sodium persulfate - sodium nitrite method[15] to a mixture of exo-4,4,8-trinitrobicyclo[3.3.0]-2,6-dioxaoctane and 4,4,8,8-tetranitrobicyclo-[3.3.0]-2,6-dioxaoctane.



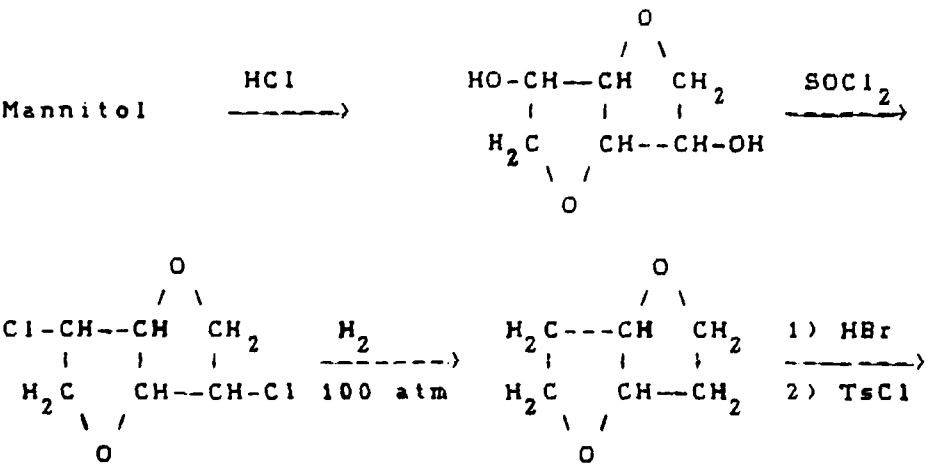
The formation of a significant amount of the trinitro derivative even in the presence of excess base and nitrating reagents indicates that the presence on the ring of the first geminal dinitro group retards the formation of the second dinitro group. The melting point of 4,4,8,8-tetranitrobicyclo[3.3.0]-2,6-dioxaoctane is 132-133 °C, with no decomposition at this temperature. The measured density is 1.78, and the calculated density is 1.79.

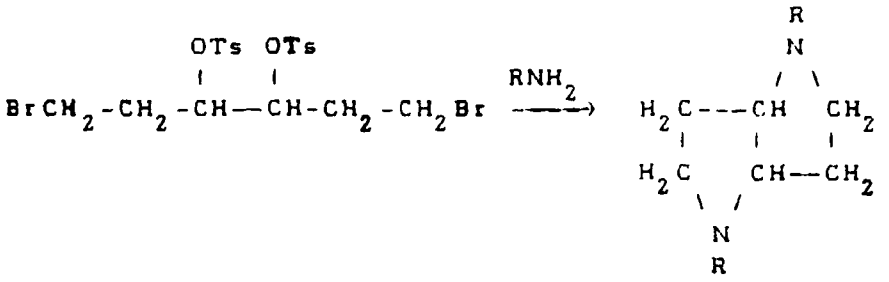
The oxime nitration route to this material was also investigated. The observed epimerization[8] of endo,endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane to the exo,exo derivative under high pressure hydrogenation, has been rationalized on the basis of a 4,8-diketo derivative.



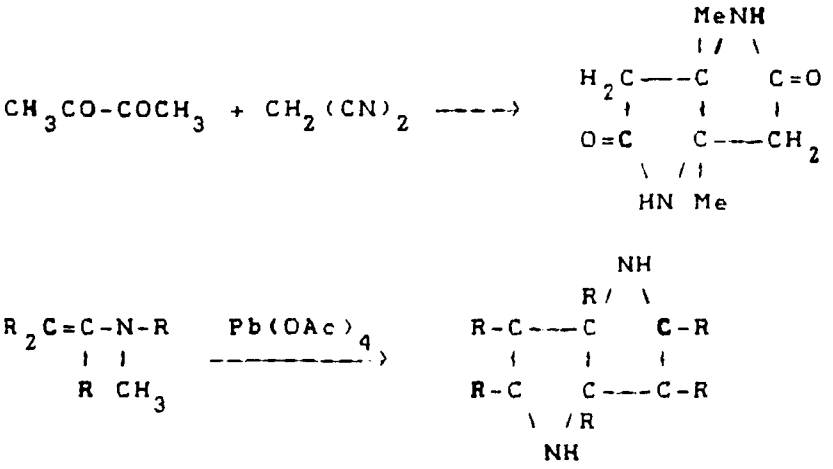
This intermediate has not been isolated. In our hands, oxidations of 4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane failed to yield the diketo compound. No carbonyl-containing materials were isolated by permanganate, silver (II) complex, oxalyl chloride - DMSO, or Jones reagent oxidation of the dihydroxy derivative. Either no reaction or complete oxidation to water soluable materials, was observed.

After 4,4,8,8-tetranitrobicyclo[3.3.0]-2,6-dioxaoctane was prepared, we turned our attention to nitro derivatives of the 2,6-diaza system. Few examples of the parent ring system are known. One example of the unfunctionalized system was prepared[9] by converting endo,endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane to the exo,exo-dichloride. The halogens were removed by high pressure hydrogenation. The remaining hydrogenated bicyclic furan was opened with gaseous hydrogen bromide, followed by preparation of the ditosylate and finally reaction with primary amines.

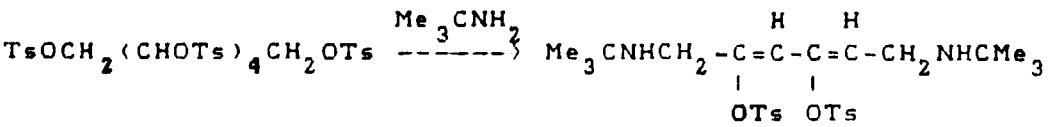




This route does not lend itself readily to the synthesis of our target compound because of problems in introducing the necessary functionality. Two other examples of the ring system are known, one prepared by a condensation of malonitrile with biacetyl[10] and the other by the lead tetraacetate oxidation of enamines[11]. Both of these routes suffer from low yields and unwanted alkyl functionality at brigehead carbons.



Our initial attempts to prepare this ring system with the necessary functionality were based on the reaction of amines with hexane derivatives with a leaving group on each carbon. The reaction of D-mannitol hexatosylate with t-butyl amine was found to give a diamine. However, elimination rather than cyclization took place, and 1,6-di-t-butylamino-2-4-di(p-toluenesulfonato)hexa-2,4-diene was isolated.



cooled. The mixture was poured into 300 mL of water and extracted 2 x 50 mL of methylene chloride. Evaporation of the solvent gave 2.3 g (80%) of N-benzylacetamide, identified by mp and NMR comparison with authentic material

The reaction of t-butylamine under similar conditions gave a 75% yield of N-t-butylacetamide.

3,4-Di(methanesulfonato)hexa-1,5-diene. A solution of 22 g (0.2 mol) of 3,4-dihydroxyhexa-1,5-diene and 60 mL of triethylamine in 200 mL of methylene chloride, was cooled to -10°C and 50 g (0.4 mol) of methanesulfonyl chloride added dropwise at a rate such that the temperature did not rise above 0°C. The mixture was then stirred at -5°C for 3 h, filtered and washed with 2 x 100 mL water. The methylene chloride solution was dried over magnesium sulfate and evaporated in vacuo (maximum temperature 30°C) to yield 38 g (70%) of crude 3,4-di(methansulfonato)hexa-1,5-diene. This material was extremely unstable even at -10°C. Samples left at room temperature capriciously decomposed with violent exotherms and black smoke evolution after 15 min to 2 weeks. Distillation of a small sample gave a few drops of 3,4-dimethansulfonatohexa-1,5-diene, bp 45-47°C (0.1 mm). Continued distillation resulted in violent exothermic decomposition. The distilled sample also decomposed within one day. This material was too unstable for elemental analysis: NMR ($CDCl_3$): δ 3.0 (6 H), 5.0-6.0 (8 H) ppm.

3,4-Di(methansulfonato)hexa-1,5-diene diepoxide. A solution of freshly prepared 3,4-di(methansulfonato)hexa-1,5-diene, (27 g, 0.1 mol) and 60 g (0.3 mol) of 85% m-chloroperbenzoic acid in 200 mL of methylene chloride was refluxed for 12 h. Then, an additional 10 g (0.05 mol) of m-chloroperbenzoic acid was added and refluxing continued for 4 h. The solution was cooled and washed with 2x100 mL 5% sodium carbonate

(8 H) ppm.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.76; H, 7.21.

3,4-Diacetoxyhexa-1,5-diene Diepoxide. A solution of 16.0 g (0.1 mol) of 3,4-diacetoxyhexa-1,5-diene and 50 g (approximately 0.25 mol) of 85% m-chloroperbenzoic acid in 100 mL of methylene chloride, was refluxed for 24 h. NMR analysis of the mixture showed the presence of 15% unreacted olefin. The mixture was then refluxed with an additional 10 g of m-chloroperbenzoic acid for 2 h. The solution was cooled, washed successively with 100 mL water, 100 mL 5% sodium hydroxide solution and 2 x 50 mL of water. Evaporation of the methylene chloide in vacuo gave 19.2 g (95%) of 3,4-diacetoxyhexa-1,5-diene diepoxide, an oil: IR (CH_2Cl_2): 3000(C-H), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (s, 6 H), 2.8 (m, 4 H), 3.1 (m, 2 H), 5.0 (m, 2 H) ppm.

Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.11; H, 6.07.

Repetition of this reaction in refluxing dichloroethane gave a 40% yield of impure product. Reaction at room temperature over several days gave mostly unreacted starting matrial with a 20% yield of 3,4-diacetoxyhexa-1,5-diene monoepoxide, bp 106-108 °C (0.3 mm): NMR ($CDCl_3$): δ 2.1 (s, 6 H), 2.8 (2 H), 3.0 (1 H), 5.0 - 5.6 (5 H) ppm.

Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.06; H, 6.49. Found: C, 56.21; H, 6.43.

Reaction of 3,4-Diacetoxyhexa-1,5-diene diepoxide with Amines. A solution of 3.8 g (0.02 mol) of 3,4-diacetoxyhexa-1,5-diene diepoxide in 50 mL of p-dioxane was reacted with 6.0 g (0.06 mol) of benzylamine added dropwise at reflux. The heating was continued for 12 h, and the solution

incorporation was observed.

3,4-Di(p-toluenesulfonato)hexa-1,5-diene. A solution of 11.4 g (0.1 mol) of 3,4-dihydroxyhexa-1,5-diene in 200 mL of dry pyridine was cooled to 5 °C and 38.0 g (0.2 mol) of p-toluenesulfonyl chloride was added. The mixture was stirred at room temperture for 48 h and poured into 2 L of water. The solid which formed was collected and recrystallized from ethanol to yield 4.0 g (10%) of 3,4-di(p-toluenesulfonato)-hexa-1,5-diene, mp 124-126 °C: NMR ($CDCl_3$) δ 2.4 (s, 6 H), 5.8-5.4 (8 H), 7.2 and 7.6 (d, Ar, 8 H) ppm.

Anal. Calcd for $C_{20}H_{22}O_6S_2$: C, 56.87; H, 5.25. Found: C, 56.96; H, 5.12.

Reaction of 3,4-Di(p-toluenesulfonato)hexa-1,5-diene with t-butylamine. A solution of 2.0 g (0.005 mol) of 3,4-di(p-toluenesulfonato)-hexa-1,5-diene and 5 mL of t-butylamine in 100 mL of p-dioxane, was refluxed for 48 h. The solution was filtered to remove 0.9 g (40%) of t-butylammonium p-toluenesulfonate. The solvent was evaporated in vacuo and the residual solid washed with 2 x 50 mL of water. Recrystallization from ethanol gave 0.55 g (28%) of the starting material, 3,4-di-p-toluenesulfonatohexa-1,5-diene, identified by mp and NMR comparison with authentic material. No amine containing products were observed.

3,4-Diacetoxyhexa-1,5-diene. Acetic anhydride (120 mL) containing a drop of concentrated sulfuric acid, was cooled to 10 °C and 34.2 g (0.3 mol) of 3,4-dihydroxyhexa-1,5-diene added slowly at a rate such that the temperature did not exceed 20 °C. After 1 h, the mixture was poured into 1 L of water and stirred for 30 min. The produot was extracted with 100 mL of methylene chloride, dried over magnesium sulfate and distilled to give 48 g (82%) of 3,4-diacetoxyhexa-1,5-diene, bp 90-91 °C (0.2 mm): IR (CH_2Cl_2) 3000(C-H), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.2 (s, 6 H), 5.0-6.0

The methanol was evaporated in vacuo and the remaining oil dissolved in 50 mL of methylene chloride. This solution was washed 2 X 50 mL of 10% aqueous hydrochloric acid and 100 mL of water, dried over magnesium sulfate and the solvent was evaporated in vacuo. The crude solid was recrystallized from ethanol to yield 2.5 g (76%) of 2,5-dichloro-3,4-di(methanesulfonato)hexa-1,5-diene, mp 92-94°C: NMR ($CDCl_3$) δ 3.1 (s, 6 H), 3.8 (m, 2 H), 5.8 (m, 4 H) ppm.

Anal. Calcd for $C_8H_{12}Cl_2O_6S_2$: C, 28.33; H, 3.53; Cl, 20.91. Found: C, 26.4; H, 3.20; Cl, 20.91.

NMR analysis of the crude reaction mixture show no incorporation of benzyl amine into the product.

A solution of 10 g (0.02 mol) of 1,6-dibromo-2,5-dichloro-3,4-di(methanesulfonato)hexane and 5.6 g (0.08 mol) of t-butylamine in 50 mL of dioxane was stirred at reflux for 4 h. The dioxane was evaporated in vacuo and the remaining oil dissolved in 50 mL of methylene chloride. This solution was washed 2 X 50 mL of 10% aqueous hydrochloric acid and 100 mL of water, and filtered through 10 g of silica gel. Evaporation of the methylene chloride gave a semi-solid which upon fractional crystallization from ethanol gave 3.5 g (41%) of what appears to be the mono dehydrohalogenated 6-bromo-2,5-dichloro-3,4-dimethanesulfonato-1-hexene, mp 134-135°C: NMR ($CDCl_3$) δ 3.1 (s, 3H), 3.3 (s, 3 H), 3.7 (m, 2 H), 4.1 (m, 2 H), 5.9 (q, 2 H) ppm.

Anal. Calcd for $C_8H_{13}BrCl_2O_6S_2$: C, 22.87; H, 3.09. Found: C, 23.10; H, 3.10.

Crystallization of the remaining material gave 1.4 g (15%) of 2,5-dichloro-3,4-di(methanesulfonato)hexa-1,5-diene, mp 134-135°C, identified by mp and NMR comparison with authentic material. No t-butylamine

1,6-Dibromo-2,5-dichloro-3,4-dihydroxyhexane (1,6-Dibromo-2,5-dichloro-1,2,5,6-tetradeoxy-D-iditol). Fuming aqueous hydrogen bromide, 50 mL (70% HBr), and 10 g (0.06 mol) of exo,exo-3,8-dichlorobicyclo[3,3,0]-2,6-dioxaoctane[13] were heated at 100°C for 18 h in a sealed glass tube. The mixture was cooled and poured into 50 mL of water. The solid which formed was collected and washed 3 x with 50 mL of water. Recrystallization from methylene chloride gave 18.0 g (86%) of 1,6-dibromo-2,5-dichloro-3,4-dihydroxyhexane, mp 59-60°C: NMR ($CDCl_3$) δ 3.1 (s, 2 H, exchange with D_2), 3.8 - 4.4 (8 H) ppm.

Anal. Calcd for $C_6H_{10}Br_2Cl_2O_2$: C, 20,89; H, 2.93. Found: C, 20.88; H, 3.03.

1,6-Dibromo-2,5-dichloro-3,4-dimethanesulfonatohexane (1,6-Dibromo-2,5-dichloro-3,4-dimethanesulfonato-1,2,5,6-tetradeoxy-D-iditol). A solution of 20.0 g (0.058 mol) of 1,6-dibromo-2,5-dichloro-3,4-dihydroxyhexane and 12 g (0.12 mol) of triethylamine in 150 mL of methylene chloride was cooled to -5°C and 13.6 g (0.12 mol) of methanesulfonyl chloride was added dropwise at such a rate that the reaction temperature did not exceed 0°C. After the addition was complete, the mixture was stirred for 1 h at 0°C, washed with 2 X 200 mL of water, and the solvent evaporated in vacuo. The crude solid was recrystallized from ethanol to give 16.5 g (57%) of 1,6-dibromo-2,5-dichloro-3,4-dimethanesulfonatohexane, mp 113-114°C: NMR ($CDCl_3$) δ 3.05 (s, 6 H), 3.4 - 4.0 (8 H) ppm.

Anal. Calcd for $C_8H_{14}Br_2Cl_2O_6S_2$: C,19.19; H, 2.81. Found: C, 19.40; H, 2.93.

Reaction of Amines with 1,6-Dibromo-2,5-dichloro-3,4-di(methanesulfonato)hexane. A solution of of 5.0 g (0.01 mol) of 1,6-dibromo-2,5-dichloro-3,4-di(methanesulfonato)hexane and 2.1 g (0.02 mol) of benzylamine in 50 mL of methanol were stirred for 36 h at room temperature.

sulfonato-D-mannitol in 50 mL of p-dioxane was refluxed with 7.3 g (0.1 mol) of t-butylamine for 3 h during which time t-butylammonium p-toluene-sulfonate precipated. The mixture was filtered and poured into 100 mL of water. Extraction with 100 mL of methylene chloride gave an oil which was shown by NMR analysis to contain no t-butyl groups.

1,6-Dichloro-2,3,4,5-tetra-p-toluenesulfonato-D-mannitol. A suspension of 7.0 g (0.03 mol) of 1,6-dichloro-D-mannitol[13] and 24.0 g (0.123 mol) of p-toluenesulfonyl chloride in 50 mL of dry pyridine was stirred for 2 h at room temperature and then kept for 4 days at 0°C. The mixture was then poured into 500 mL of water and extracted with 100 mL of methylene chloride. The organic solurion was washed with 5% aqueous hydrochloric acid and solvent was evaporated to yield 16.0 g (69%) of 1,6-dichloro-2,3,4,5-tetra-p-toluenesulfonato-D-mannitol, mp 133-134°C (ethanol): IR (CH_2Cl_2) 3000(C-H), 1360 cm^{-1}, NMR ($CDCl_3$) & 2.3 (s, 12H), 3.3 (m, 4H), 4.5 (m, 4H), 7.2 (ABq, 16H) ppm.

Anal. Calcd for $C_{34}H_{36}Cl_2O_{12}S_4$: C, 48.84; H, 4 34. Found: C, 48.63; H, 4.40.

Reaction of 1,6-Dichloro-2,3,4,5-tetra-p-toluenesulfonato-D-mannitol with t-butylamine. A solution of 15 g (0.02 mol) of 1,6-dichloro-2,3,4,5-tetra-p-toluenesulfonato-D-mannitol and 7.3 g (0.1 mol) of t-butylamine in 100 mL of methanol was heated in a bomb at 100°C for 3 days. The mixture was cooled and poured into 500 mL of water. Extraction with ether gave a red polymeric material which showed only a trace of t-butyl groups by NMR analysis.

When 1,6-dichloro-2,3,4,5-tetra-p-toluenesulfonato-D-mannitol was refluxed in p-dioxane with t-butylamine for 4 h, only unreacted starting material was recovered.

tetrahydrofuran was refluxed for 4 H. The mixture was poured into 500 mL of water, extracted twice with 50 mL portions of methylene chloride and stripped of solvent. Trituration of the residual oil with ethanol gave 1.0 g (5%) of starting material which was removed by filtration. The ethanol solution was evaporated under vacuum and the residual oil chromatographed on silica gel with ether to yield 4.2 g (37%) of 1,6-di-t-butylamino-2,4-di(p-toluenesulfonato)hexa-2,4-diene, mp 124-125 °C (ether - hexane); IR (CH_2Cl_2) 3400 (N-H), 3000(C-H), 1360 cm^{-1}; NMR ($CDCl_3$) δ 0.95 (s, 9 H), 1.0 (s, 9 H), 2.4 (s, 6 H), 2.9 (d, J= 2 Hz, 2 H), 3.2 (s, 2 H), 5.6 (m, 2 H), 7.2 (m, 8 H) ppm.

Anal. Calcd for $C_{28}H_{40}N_2O_6SO_2$: C, 59.49; H, 7.09; N, 4.95. Found: C, 59.61; H, 7.20; N, 4.95.

1,3,4,6-Tetra-p-toluenesulfonato-D-mannitol. A solution of 13.0 g (0.026 mol) of 3,4-di-p-toluenesulfonato-D-mannitol[12] in 100 mL of dry pyridine was cooled to 5 °C, and 9.8 g (0.052 mol) of p-toluenesulfonyl chloride was added portionwise over 10 min such that the temperature did not rise above 10 °C. The mixture was stirred for 3 h at room temperature, poured into 500 mL of water, and extracted with 2 x 100 mL of methylene chloride. The methylene chloride solution was washed with 5% aqueous hydrochloric acid (2 x 50 mL) and with water (2 x 100 mL), and the solvent was evaporated to yield 19.0 g (91%) of 1,3,4,6-tetra-p-toluenesulfonato-D-mannitol, a syrup: IR (CH_2Cl_2) 3000(C-H), 1590 (C=C), 1350 cm^{-1}; NMR ($CDCl_3$): δ 2.3 (s, 12H), 3.6 (2H, exchanges with D_2O), 3.9 (m, 8 H), 4.7 (m, 2H), 7.2 (m, 16 H) ppm.

Anal. Calcd for $C_{34}H_{38}O_{14}S_4$: C, 51.2; H, 4.76. Found: C, 51.22; H, 4.78.

Reaction of 1,3,4,6-Tetra-p-toluenesulfonato-D-mannitol with t-Butylamine. A solution of 8.0 g (0.01 mol) of 1,3,4,6-tetra-p-toluene-

100 mL of acetic acid at 25 °C and the mixture stirred for 8 h. The solution was diluted with 1 l of water, and extracted twice with 100 mL portions of methylene chloride. The combined organic layers were washed twice with 50 mL portions of 10% sodium hydroxide solution. Evaporation of the organic layer in vacuo left no residue.

Attempted oxidations with potassium permanganate in water, potassium permanganate and copper sulfate in benzene, oxallyl chloride / dimethyl-sulfoxide / triethylamine in methylene chloride, sodium bromate / cerric ammonium sulfate, or chromium trioxide in pyridine were similarly unuccessful.

. **1,2,3,4,5,6-Hexa-p-toluenesulfonato-D-mannitol**. A suspension of 18 g (0.1 mol) of D-mannitol in 500 mL of dry pyridine was cooled to 5°C, and 150 g (0.81 mol) of p-toluenesulfonyl chloride was added portionwise over 15 min at such a rate that the temperture did not rise above 10°C. This mixture was stirred for 4 h at 0 °C and then was allowed to stand at 0 °C for 7 days. The mixture was poured into 3 L of water and extracted with methylene chloride (3 x 100 mL). After the methylene chloride solution was washed twice with 100 mL portions of 5% aqueous hydrochloric acid and twice with 100 mL portions of water, the solvent was evaporated to yield 110 g of crude product. Recrystallization from methanol gave 78.0 g (71%) of 1,2,3,4,5,6-hexa-p-toluenesulfonato-D-mannitol, mp 135-136°C (lit.[12] 124-126°C); IR (CH_2Cl_2) 3000(C-H), 1590 (C=C), 1360 (S=O), 1180 cm^{-1}, NMR ($CDCl_3$) δ 2.3 (s, 18 H), 3.8 (m, 4H), 4.6 (m, 4 H), 7.3 (24 H) ppm.

Reaction of 1,2,3,4,5,6-Hexa-p-toluenesulfonato-D-mannitol with t-butylamine. A solution of 19 g (0.02 mol) of 1,2,3,4,5,6-hexa-p-toluene-sulfonato-D-mannitol and 15.6 g (0.2 mol) of t-butylamine in 100 mL of

for 1 h until the solids dissolved completely. To this solution was then added a solution of 12 g (0.17 mol) of sodium nitrite and 3 g (0.001 mol) of potassium ferrocyanide in 50 mL of water, followed by 13 g (0.07 mol) of solid sodium persulfate. The mixture was stirred for 2 h at 20°C, extracted twice with 30 mL portions of methylene chloride. The organic layer was dried with magnesium sulfate and solvent was removed in vacuo to yield 1.4 g of a semi-solid. This material was crytallized from 15 mL of carbon tetrachloride and then was sublimed. Recrystallization of the sublimate from ethanol yielded 0.85 g (24%) of 4,4,8,8-tetranitrobicyclo[3.3.0]-2,6-dioxaoctane, mp 131-133°C, density 1.795 (silver nitrate flotation): IR (CH_2Cl_2): 3000(C-H), 1580, 1420(NO_2), 1310, 1240, 1100, 920 cm^{-1}; NMR ($CDCl_3$) δ 5.6 (s, 2 H), 4.9 (d, 1 H, J = 6 Hz) and 4.6 (d, 1 H, J= 6 Hz) ppm.

Anal. Calcd for $C_6H_6N_4O_{10}$: C, 24.50; H, 2.04, N, 19.05. Found: C, 25.65; H, 2.11; N, 17.72.

The mother liquor was chromatographed on silica gel with 10% ethyl acetate / hexane to yield 0.15 g (5%) of exo-4,4,8-trinitrobicyclo-[3.3.0]-2,6-dioxaoctane. This material was sublimed at 70°C (0.1 mm) and then recrystallized from hexane: mp 93-95°C; density 1.58 (silver nitrate flotation); IR (CH_2Cl_2): 3000(C-H), 1580, 1480(NO_2), 1370, 1320, 1110, 920 cm^{-1}; NMR ($CDCl_3$): δ 4.15 (d, 2 H, J= 1 Hz), 4.35 (m, 2 H), 4.6 (m, 1 H), 4.95 (d, 1 H, J = 1.5 Hz), 5.45 (d, 1 H, J = 1.5 Hz).

Anal. Calcd for $C_6H_7N_3O_8$: C, 28.92; H, 2.83; N, 16.86. Found: C, 29.10; H, 2.99; N, 16.53.

Attempted oxidation of endo,endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane. A solution of 14.6 g (0.1 mol) of endo,endo-4,8-dihydroxy-bicyclo[3.3.0]-2,6-dioxaoctane in 100 mL of glacial acetic acetic acid was added slowly to a solution of 20 g (0.2 mol) of chromium trioxide in

This crude material was recrystalized from methylene chloride / carbon tetrachloride (50:50) to yield 6.4 g (88%) of the hygroscopic exo,exo-4,8-diaminobicyclo[3.3.0]-2,6-dioxaoctane mp 75-77 °C, (literature[7] mp 57-59 °C), bp 107-110 °C (0.1 mm): IR (CH_2Cl_2) 3400(N-H), 3000, 2950(C-H), 1270, 1180, 1060 cm^{-1}; NMR: ($CDCl_3$) δ 1.4 (s, 4 H, exchange with D_2O), 3.3 (m, 4 H), 3.7 (m, 2 H), 4.2 (s, 2 H) ppm.

Anal. Calcd for $C_6H_{12}N_2O_2$: C, 49.98; H, 8.39. Found: C, 49.71; H, 8.51.

Exo,exo-4,8-dinitrobicyclo[3.3.0]-2,6-dioxaoctane. A solution of 20 g (approx. 0.1 mol) of 85% m-chloroperoxybenzoic acid in 200 mL of dichloroethane was heated to reflux, and a solution of 2.0 g (0.0014 mol) of exo,exo-4,8-diaminoobicyclo[3.3.0]-2,6-dioxaoctane in 10 mL of dichloroethane was added dropwise. Refluxing was continued for 4 h, and the initially green solution became colorless. The solution was then cooled, filtered and washed twice with 50 mL portions of 10% sodium hydroxide solution. The organic layer was dried over magnesium sulfate and the solvent was evaporated in vacuo. Sublimation of the residue at 100 °C (0.1 mm) yielded 0.9 g (32%) of exo,exo-4,8-dinitrobicyclo[3.3.0]-2,6-dioxaoctane, mp 87-88 (from carbon tetrachloride): IR (CH_2Cl_2): 3150, 3000(C-H), 1580, 1420(NO_2), 1380, 1360, 1280, 1100, 900 cm^{-1}; NMR ($CDCl_3$): δ 4.0 (m, 4 H), 4.9 (m, 2 H), 5.05 (s, 2 H) ppm.

Anal. Calcd for $C_6H_8N_2O_6$: C, 35.30; H, 3.95; N, 13.72. Found: C, 35.72; H, 3.90; N, 13.43.

4,4,8,8-Tetranitrobicyclo[3.3.0]-2,6-dioxaoctane and Exo-4,4,8-trinitrobicyclo[3.3.0]-2,6-dioxaoctane. A solution of 1.2 g (0.3 mol) of sodium hydroxide in 50 mL of water and 15 mL of methanol was stirred with 2.4 g (0.015 mol) of exo,exo-4,8-dinitrobicyclo[3.3.0]-2,6-dioxaoctane

The methylene chloride solution was washed twice with water, dried over magnesium sulfate and evaporated to yield 38 g (96%) of starting material identified by nmr and ir. No trace of nitro absorbtion was observed in the ir spectrum.

Reaction of endo,endo-4,8-dimethanesulfonatobicyclo[3.3.0]-2,6-dioxaoctane with sodium nitrite at 70 °C led to similar results. At reaction temperatures above 120 °C, no starting materials were recovered.

Exo,exo-4,8-diazidobicyclo[3.3.0]-2,6-dioxaoctane. A mixture of 41 g (0.08 mol) of endo,endo-4,8-di-p-toluenesulfonatobicyclo[3.3.0]-2,6-dioxaoctane, 20 g (0.3 mol) of sodium azide and 200 mL of diethyleneglycol was heated at 135 °C for 5 hours. The mixture was cooled, poured into 1 L of water, and the product was extracted three times with 50 mL portions of methylene chloride. The organic layer was separated, dried over magnesium sulfate and filtered through 10 g of silica gel to yield 9.0g (50%) of essentially pure exo,exo-4,8-diazidobicyclo[3.3.0]-2,6-dioxaootane. A small amount of this material was distilled (bp 92-94 °C / 0.3 mm) to give an analytical sample; IR (CH_2Cl_2): 3100, 3000, 2950(C-H), 2150($-N_3$), 1360, 1270, 1180, 1100, 1040, 1020, 900 cm^{-1}; NMR ($CDCl_3$): δ 3.8 (m, 4 H), 4.05 (m, 2 H), 4.5 (s, 2 H) ppm.

Anal. Calcd for $C_6H_8N_6O_2$: C, 36.73; H, 4.11; N, 42.84. Found: C, 36.67; H, 4.12; N, 42.17.

Exo,exo-4,8-diaminobicyclo[3.3.0]-2,6-dioxaoctane. A mixture of 9.8 g (0.05 mol) of exo,exo-4,8-diazidobicyclo[3.3.0]-2,6-dioxaoctane and 1.0 of 5% palladium on carbon in 100 mL of methanol was hydrogenated at 40 psi in Parr bomb. The bomb was evacuated and repressurized three times during 12 h until the infrared spectrum of an aliquot no longer showed azide absorption between 2300 and 2150 cm^{-1}. After the catalyst was filtered off, the solvent was evaporated in vacuo to give a waxy solid.

methylene chloride. The methylene chloride solution was washed with three 250 mL portions of water, dried over magnesium sulfate and stripped of solvent to give 49g (96%) of endo,endo-4,8-Di-p-toluenesulfonatobicyclo[3.3.0]-2,6-dioxaoctane, mp 88-90°C (ethanol), (literature[5] mp 89-90°C): IR (CH_2Cl_2): 3000, 2950, 1400, 1260, 1100 cm^{-1}; NMR ($CDCl_3$): δ 2.4 (s, 6 H), 3.8 (m, 4 H), 4.4 (m, 2 H), 4.8 (m, 2 H), 7.2 and 7.7 (d, 8 H, J= 4.5 Hz) ppm.

Endo,endo-4,8-dimethanesulfonatobicyclo[3.3.0]-2,6-dioxaoctane. A solution of 42 g (0.3 mol) of endo,endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane and 100g (1.0 mol) of triethylamine in 500 mL of benzene was cooled to 0°C. Methanesulfonyl chloride (80 g, 0.7 mol) was added dropwise at a rate such that the temperature did not rise above 5°C. The mixture was allowed to stand at 0°C overnight and was filtered. The benzene solution was washed twice with 200 mL of water and evaporated to give an oil, which crystallized on trituration with methylene chloride. Recrystallization of this solid from methanol gave 57 g (61%) of endo,-endo-4,8-dimethanesulfonatobicyclo[3.3.0]-2,6-dioxaoctane, mp. 98-99°C: IR (CH_2Cl_2): 3000, 2950(C-H), 1375, 1180, 1050, 980 cm^{-1}; NMR ($CDCl_3$) δ 3.0 (s, 6 H), 3.9 (m, 4 H), 4.5 (m, 2 H), 4.9 (m, 2 H) ppm.

Anal. Calcd for $C_8H_{14}S_2O_8$: C, 31.78; H, 4.67. Found: C, 31.69; H, 4.61.

Reaction of endo,endo-4,8-di-p-toluenesulfonatobicyclo[3.3.0]-2,6-dioxaoctane with nitrite. A solution of 40 g (0.088 mol) of endo,endo-4,8-di-p-toluenesulfonatobicyclo[3.3.0]-2,6-dioxaoctane in 200 mL of dimethylformamide, was reacted with 14 g (0.2 mol) of sodium nitrite and 25 g (0.15 mol) of phloroglucinol at 70°C for 48 hours. The mixture was poured into 1 L of water and extracted with 100 mL of methylene chloride.

hexane diepoxide gave a small yield of methanesulfonyl azide. However, 1,6-dibromo-2,3,4,5-tetraacetoxy-D-mannitol reacted with sodium azide to give a 50% yield of 1,6-diazido-2,3,4,5-tetraacetoxy-D-mannitol. The reduction of the azide groups and cyclization to the desired ring system will be studied.

$$Br-CH_2-(CH-OAc)_4-CH_2-Br \xrightarrow{N_3^-} N_3-CH_2-(CH-OAo)_4-CH_2-N_3$$

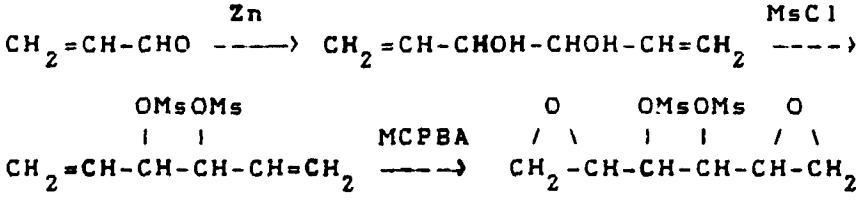
B. EXPERIMENTAL

Endo,endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane. In a modification of the procedure of Wiggins[4], a solution of 500 g of mannitol in 3 L of 35% hydrochloric acid was refluxed for 4 days. The reaction mixture was concentrated at 100°C under water aspirator vacuum to give a syrup, which was redissolved in 300 mL of water, and reconcentrated under the same conditions. The syrup was distilled and the fraction boiling at 120 - 160°C (0.2 mm) was redistilled to give 120 g (25%) of endo,endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane, an oil, bp 130-140°C (0.2 mm) which crystallized upon seeding to yield a colorless solid, mp 85-86°C (literature[1] mp 87°C): IR (CH_2Cl_2): 3600(O-H), 3000(C-H), 1400, 1080 cm^{-1}; NMR ($CDCl_3$): δ 3.6 - 4.4 (m) ppm.

Endo,endo-4,8-di-p-toluenesulfonatobicyclo[3.3.0]-2,6-dioxaoctane. A solution of 14.6 g (0.1 mol) of endo,endo-4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane in 200 ml of pyridine was cooled to 5°C with an ice bath and 50.0 g (0.21 mol) of solid p-toluenesulfonyl chloride was added over 15 minutes. The mixture was stirred for 24 hours at 5°C and then was poured into 1 L of water. The product was extracted with 100 ml of

With 1,3,4,6-tetra-p-toluenesulfonato-D-mannitol, or 1,6-dichloro-2,3,4,5-tetra-p-toluenesulfonato-D-mannitol, tars were obtained with no amine incorporation. The compound 1,6-dibromo-2,5-dichloro-3,4-dimethanesulfonato-D-mannitol underwent elimination with t-butylamine to give 6-bromo-2,5-dichloro-3,4-dimethanesulfonato-1-hexene.

Several disubstituted hexane diepoxides were prepared and reacted with amines. Reactions of 3,4-dihydroxy-1,5-hexane diepoxide and amines resulted either in hydrolysis to D-mannitol or rearrangement to 4,8-dihydroxybicyclo[3.3.0]-2,6-dioxaoctane. This diepoxide was so prone to base catalyzed rearrangement that it could not be converted directly to its methanesulfonate or tosylate. To prepare these materials, acrolein was dimerized to 3,4-dihydroxyhexa-1,5-diene. The hydroxyl groups of this compound were then reacted with methanesulfonyl chloride to form the 3,4-dimethanesulfonatohexa-1,5-diene, which was epoxidized with m-chloroperbenzoic acid to the desired diepoxides. By a similar series of reactions, 3,4-di-acetoxy-1,5-hexane diepoxide was made.



Reaction of the 3,4-diacetoxy diepoxide with t-butyl amine or benzyl amine gave high yields of N-alkyl acetamides. Thus, reaction occurred preferentially at the acetate group over epoxide opening. In the case of the 3,4-dimethansulfonate diepoxide, some amine incorporation was observed, but no diamine adduct was isolated.

The reaction of hexa-p-toluenesulfonato-D-mannitol with sodium azide gave only a polymeric residue from which no useful materials could be isolated. Reaction of sodium azide with 3,4-dimethanesulfonato-1,5-

solution and 2 x 100 mL of water. After the mixture was dried over magnesium sulfate, solvent was evaporated in vacuo to give an oil which solidified. Recrystallization from ethanol gave 31 g (38%) of 3,4-di(methansulfonato)hexa-1,5-diene diepoxide as a mixture of isomers, mp 85-95°C; NMR ($CDCl_3$) δ 2.8 (4 H), 3.1 (s, 6 H), 3.2 (m, 2 H), 4.6 (m, 2) ppm.

Anal. Calcd for $C_8H_{14}O_6S_2$: C, 35.54; H, 5.22. Found: C, 35.68; H, 5.35.

Attempted preparation of this material in refluxing dichloroethane lead to violent decomposition of the starting material. At room temperature, no reaction was observed.

1,6-diazido-2,3,4,5-tetraacetoxy-D-mannitol. A solution of 5.7 g (0.01 mol) of 1,6-dibromo-2,3,4,5-tetraacetoxy-D-mannitol[14] and 3.4 g (0.05 mol) of sodium azide in 30 mL of diethylene glycol, was heated at 100°C for 6 h. Th solution was cooled and poured into 500 mL of water and extracted with 3 X 100 mL of methylene chloride. The methylene chloride solutions were combined, dried over magnesium sulfate and evaporated in vacuo. Column chromatography on silica gel (hexane - ethyl acetate, 90:10) gave 2.0 g (50%) of 1,6-diazido-2,3,4,5-tetraacetoxy-D-mannitol, an oil: IR (CH_2Cl_2) 3000(C-H), 2150 (N_3), 1720 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.1 (s, 12 H), 3.5 (t, 4 H), 5.0-5.4 (m, 4 H) ppm

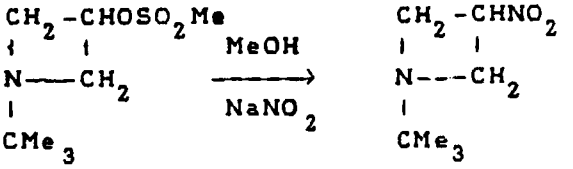
Anal. Calcd for $C_{14}H_{20}N_6O_8$: C, 41.99; H, 5.03; N, 20.99. Found: C, 41.90; H, 5.09; N, 19.96.

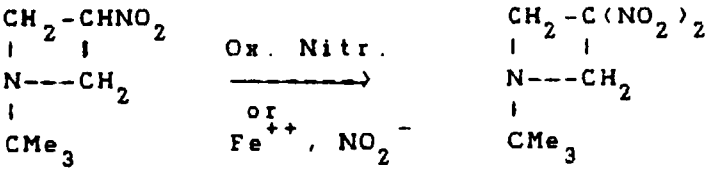
In refluxing acetone, 1,6-dibromo-2,3,4,5-tetraacetoxy-D-mannitol did not react with sodium azide.

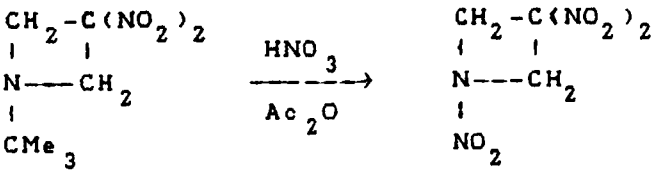
III. AZETIDINE AND DIAZETIDINE CHEMISTRY

A. DISCUSSION

During the preceeding year, we synthesized 1,3,3-trinitroazetidine by the following reaction sequence.



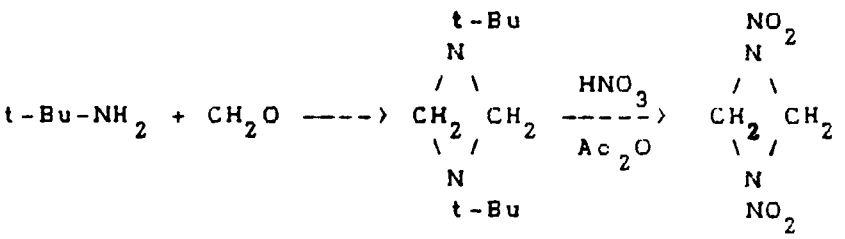




Several improvements in the preparation of 1,3,3-trinitroazetidine have been made. It was found that substitution of methylene chloride for benzene in the preparation of the 1-t-butyl-3-methanesulfonatoazetidine increased the yields to 90%. Oxidative nitration of the mononitro derivative without prior purification was carried out using the potassium ferrocyanide - sodium persulfate - sodium nitrite method. This change eliminated the need to distill the unstable and potentially explosive mononitro derivative and improved the overall conversion. However, several variations of reaction conditions did not improve significantly the yield for the sodium nitrite - methanesulfonate reaction to afford the mono nitroazetidine. The improve sequence was used to prepare 5 g of 1,3,3-trinitroazetidine for testing. Experimental details of the changes are included in Appendix A.

On the basis of several reports in the literature of stable 1,3-diazetidenes, we attempted to synthesize 1,3-dinitro-1,3-diazetidine. This material is of interest as the smallest member of the $(CH_2\text{-}N(NO_2))_n$ family, which includes RDX and HMX.

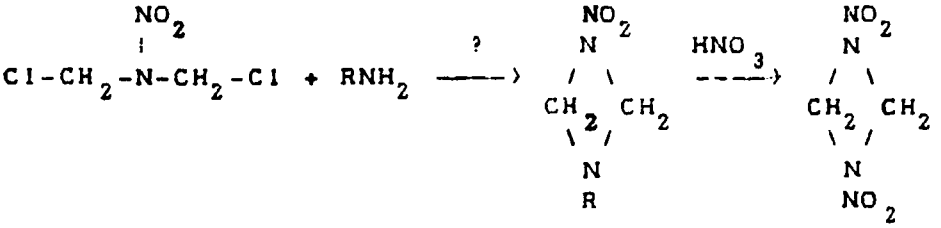
Although peaks for 1,3-dinitro-1,3-diazetidine has been reported in the mass spectrum of HMX[16], the compound has not been isolated. Cyclohexylamine and t-butylamine have been reported to react with formaldehyde with elimination of water to yield the the monomeric methylene imines, which then dimerized to the 1,3-dialkyl-1,3-diazetidine[17,18] It was expected that direct nitrolysis of 1,3-di-t-butyl-1,3-diazetidine might yield the desired product directly.



In our hands, the reaction of cyclohexylamine with formaldehyde gave only the known 1,3,5-tricyclohexyl-s-triazine[19]. In the reaction of t-butylamine with formaldehyde, the freshly distilled product showed only one methylene absorbance in the NMR at δ3.45 ppm, consistent with reported NMR values for s-triazines[19]. In several hours, new NMR signals appeared at δ 7.05 ppm, indicative of monomeric t-butylmethyleneimine[20]. After 2 days, equilibrium is reached at approximately 50% monomer and 50% trimer, and no absorbance indicative of dimer was observed. Direct nitration of this material gives no new nitramines.

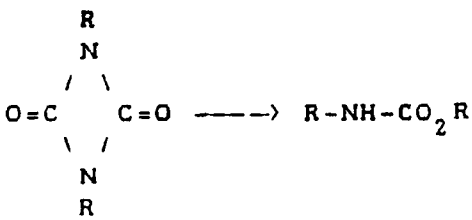
Another approach to 1,3-diazetidines that was examined is the reaction of 1,3-dichloro-2-nitro-2-azapropane[21] with amines to form mono-

nitro diazetidines, followed by nitrolysis.



Although this dichloride is known to undergo displacement reactions with azide to form 1,3-diazido-2-nitro-2-azapropane[21], no displacements with amines were observed, and the starting material was decomposed.

Another potential route to 1,3-diazetidines is hydrogenolysis of uretidones. These materials are quite susceptable to ring opening and attempted hydrogenolysis of 1,3-dibenzyhdryl uretidone[22] or 1,3-di-t-butyluretidone[23] in alcohol gave only the carbamates.



B. EXPERIMENTAL

Reaction of 1,3-dichloro-2-nitro-2-azapropane with Benzhydrylamine. To a solution of 1.5 g (0.01 mol) of 1,3-dichloro-2-nitro-2-azapropane[21] dissolved in 5 mL of triethylamine at -10 °C, was added dropwise 1.75 g (0.009 mol) of benzhydrylamine. After 10 min, the mixture solidified and 10 mL of water and 25 mL of methylene chloride were added. The organic layer was dried over magnesium sulfate. Evaporation of the solvent in vacuo gave a solid which was recrystallized from ethanol to give 0.85 g (50%) of 1,3,5-tribenzyhdryl-1,3,5-triazine, mp 204-206, identical with

authentic material made from benzhydrylamine and formaldehyde. NMR ($CDCl_3$) δ 3.2 (m, 6H), 4.5 (s, 3H), 7.0 (m, 30 H) ppm.

Anal. Calc for $C_{42}H_{39}N_3$: C, 86.11; H, 6.71 Found: C, 86.51; H, 6.58.

Reaction of 1,3-Dichloro-2-nitro-2-azapropane with t-Butylamine. A solution of 0.73 g (0.01 mol) of t-butylamine in 5 mL of acetic acid was stirred with 1.5 g (0.01 mol) of 1,3-dichloro-2-nitro-2-azapropane at room temperature for 48 h. NMR analysis of the reaction mixture showed no reaction had occurred. Next 2 mL of triethylamine was added and the mixture heated to 80°C for two h, cooled and the solvent evaporated to yield 0.80 g (40%) of 1,3-diacetoxy-2-nitro-2-azapropane[21], identified by NMR and melting point comparison with authentic material.

Reaction of 1,3-Dichloro-2-nitro-2-azapropane with Ammonia. A solution of 0.7 g (0.005 mol) of 1,3-dichloro-2-nitro-2-azapropane in 20 mL of liquid ammonia was refluxed for 3 hours. Evaporation of the solvent left only 0.37 g (70%) of ammonium chloride.

Reaction of 1,7-Diacetoxy-2,4,6-trinitro-2,4,6-triazaheptane with t-Butylamine. A solution of 1.2 g (0.003 mol) of 1,7-diacetoxy-2,4,6-trinitro-2,4,6-triazaheptane in 20 mL of acetone was stirred 16 h with 10 mL of t-butylamine. The highly crystalline material which formed was filtered to yield 0.75g (95%) of RDX, mp 200°C(dec), as identified by mp and NMR comparison with authentic material.

Reaction of 1,3-Diacetoxy-2-nitro-2-azapropane with t-Butylamine. A solution of 5.0 g (0.025 mol) 1,3-diacetoxy-2-nitro-2-azapropane in 30 mL of acetone was stirred with 2.0 g (0.025 mol) of t-butylamine for 24 h at room temperature. The t-butylammonium acetate which formed was filtered. Evaporation of the solvent in vacuo left a small amount of unreacted starting material.

Attempted Preparation of 1,3-Di-t-butyl-1,3-diazetidine. A mixture of 36 g (0.5 mol) of t-butylamine and 15 g (0.5 mol) of paraformaldehyde in 200 mL of benzene containing 1 drop of concentrated sulfuric acid, was refluxed until 8.6 mL of the water azeotrope was collected in a Dean Stark trap. The benzene was evaporated and the remaining oil distilled to yield 10.0 g of 1,3,5-tri-t-butyl-1,3-5-triazine, bp. 35-38 (200 mm). The NMR spectrum (neat)of the freshly distilled sample showed δ 1.05 (s, 9 H) and 3.5 (s, 2 H). Upon standing new absorbances attributable to the monomeric t-butylmethylene amine at 1.10 (s) and 7.05 (d) arose. After 2 days the spectrum showed approximately a 50:50 mixture of monomer and trimer. No evidence was observed for the reported dimeric 1,3-di-t-butyl-1,3-diazetidine.

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Synthesis of Nitro-Substituted Azetidines[1]

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ABSTRACT

The reaction of sodium nitrite with 1-t-butyl-3-methanesulfonatoazetidine gave 1-t-butyl-3-nitroazetidine. Oxidative nitration gave 1-t-butyl-3,3-dinitroazetidine, and subsequent nitrolysis with nitric acid - acetic anhydride gave 1,3,3-trinitroazetidine. 1-Benzhydryl-3,3-dinitroazetidine was obtained from 1-benzhydryl-3-methanesulfonatoazetidine by nitrite displacement followed by oxidative nitration. 1-t-Butyl-3-(methanesulfonato)azetidine reacted with sodium azide to give 1-t-butyl-3-azidoazetidine. Nitration of 1-t-butyl-3-hydroxyazetidine, 3-methanesulfonatoazetidine, 3-carboxyazetidine and 3-hydroxyazetidine gave, respectively, 1-t-butyl-3-nitratoazetidine, 1-nitro-3-methanesulfonatoazetidine, 3-carboxy-1-nitroazetidine and 1-nitro-3-nitratoazetidine. 1-Nitroazetidines with leaving groups at the 3- position did not undergo displacement reactions, apparently because transanular assistance by an electron-rich nitrogen is needed.

Although a considerable amount of work dealing with azetidines has been reported,[2] the only nitro-substituted example known is 1-nitroazetidine, which was synthesized from 1-nitrosoazetidine by pertrifluoroacetic acid oxidation.[3] In a preceeding paper, we reported the preparation of 3,3-dinitrooxetane.[4] In a continuation of our investigations of electon-deficient small ring heterocycles, we have studied the synthesis of nitro-substituted azetidines, with particular interest in preparing 1,3,3-trinitroazetidine (1), the nitramine analog of 3,3-dinitrooxetane.

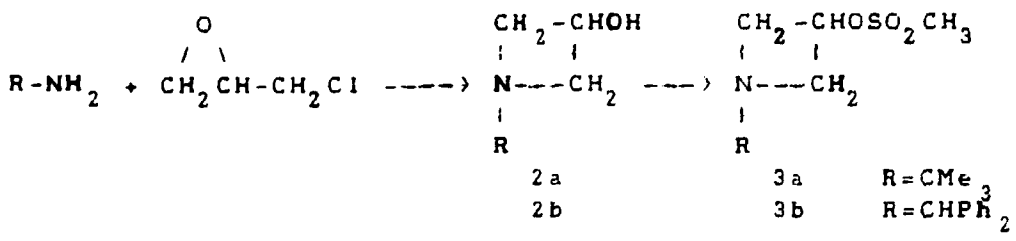
In our experience with the preparation of dinitrooxetane, we found that a nitro group could not be introduced at the 3 position by displacements with sodium nitrite. We also note that nitrocyclobutanes have not been reported by direct nitrite displacement.

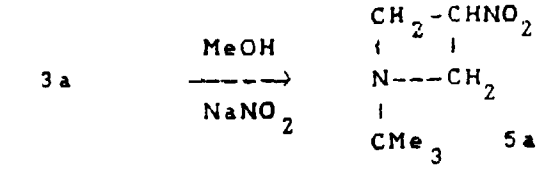
Displacement reactions at C-3 in 1-alkyl-3-p-toluenesulfonatoazetidines have been shown to proceed via 1-azoniumbicyclo[1.1.0]butane intermediates. This participation by the ring nitrogen of the azetidine causes rate enhancements in solvolysis reactions compared to cyclobutyl tosylate.[5,6] It therefore seemed possible that participation by the azetidine nitrogen would facilitate nitrite displacement. This participation, which depends on the electron density at nitrogen, was not observed when the azetidine nitrogen carried a p-toluenesulfonyl group[7].

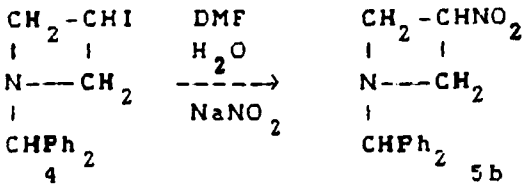
N-Alkyl substituted azetidines with functional groups at C-3 are readily accessible by the reactions of primary amines with epichlorohydrin.[8] For this study, it was desirable to utilize an N-alkyl group that can be converted readily to an N-nitro group The N-benzhydryl group undergoes hydrogenolysis conveniently to give the free secondary amine[9], and the N-t-butyl group is converted directly to the n-nitro group in other heterocyclic systems by nitrolysis[10]. Thus 1-t-butyl-3-

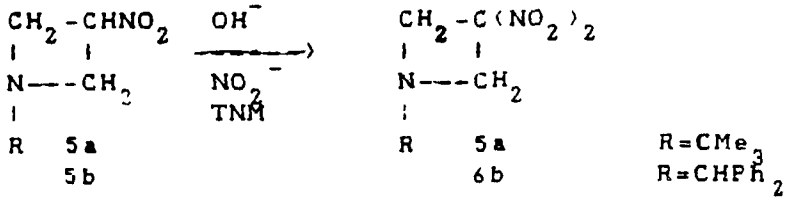
hydroxyazetidine (2a) and 1-benzhydryl-3-hydroxyazetidine (2b) were selected as starting materials.

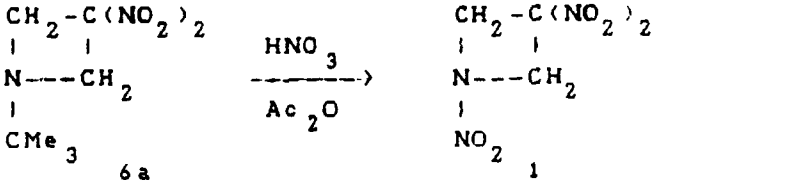
Reactions of 1-t-butyl-3-hydroxyazetidine (2a) and 1-benzhydryl-3-hydroxyazetidine (2b) with methanesulfonyl chloride[11] gave the corresponding 3-methanesulfonates (3a,b). The direct displacement of these methanesulfonates groups by sodium nitrite was found to produce the 3-nitroazetidines (5a,b) under rather specific conditions. The reaction of the t-butyl compound (3a) at $0^{\circ}C$ with sodium nitrite in aqueous methanol containing phloroglucinol dihydrate gave an 8% yield of 1-t-butyl-3-nitroazetidine (5a) in 48 h. This material was somewhat unstable, and reactions at higher temperatures or in more ionizing solvents such as DMF yielded no product. The less reactive 1-t-butyl-3-bromo or 3-p-toluenesulfonatoazetidine derivatives failed to give this product. Under these conditions the benzhydryl-substituted methansulfonate (3b) did not give the substitution product (5b). However, (5b) was obtained in 11% yield from the 3-iodoazetidine (4) and sodium nitrite in aqueous DMF at $50^{\circ}C$ in the presence of phloroglucinol. Compound (5b) was also obtained from compound (4) formed in-situ from the methanesulfonate (3b) and sodium iodide. These reactions represent the first examples of nitrite displacements on four-membered rings.









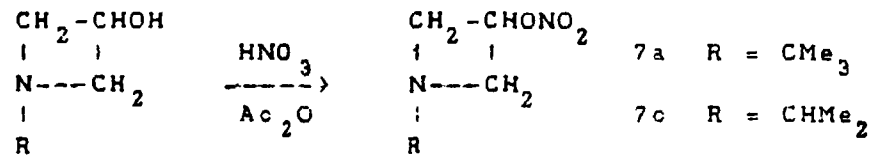


Attempts to effect oxidative nitration of 1-benzhydryl-3-nitroazetidine (5b) with silver nitrate - sodium nitrite were unsuccessful because of low water solubility of the nitronate salt. However, the gem-dinitro derivative (6b) was produced from (5b) in 38% yield by reacting its nitronate salt with sodium nitrite and tetranitromethane in ethanol. On the other hand, the t-butyl derivative (5a) was oxidatively nitrated with

silver nitrate and sodium nitrite to give 1-t-butyl-3,3-dinitroazetidine (6a) in 39% yield. Compound (6a) was obtained in 60% yield with a recently developed procedure[12] in which the nitronate salt was reacted with potassium ferrocyanide, sodium persulfate and sodium nitrite.

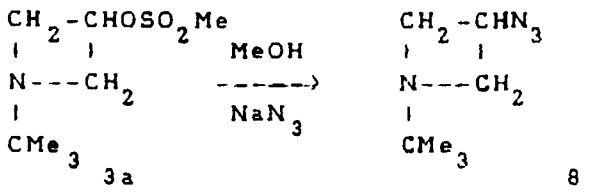
Attempts to convert 1-benzhydryl-3,3-dinitroazetidine (6b) to 1,3,3-trinitroazetidine (1) were unsuccessful. Although the hydrogenolysis of (6b) was found to give an 80% yield of diphenylmethane, no nitro-containing compounds were isolated. Direct nitration also failed to give (1). On the other hand, 1-t-butyl-3,3-dinitroazetidine (6a) was found to form stable salts with strong acids, and was thus resistant to nitrolysis even with hot mixed nitric and sulfuric acids. With 100% nitric acid, the nitrate salt of (6a) was obtained. The corresponding triflate salt and the hydrobromide were also isolated. Compound (6a) reacted with bromine to give a stable 1:1 adduct from which it could be regenerated. However, (6a) reacted quickly with nitric acid and acetic anhydride at $0\,^{\circ}C$ to give a 35% yield of 1,3,3-trinitroazetidine (1).

It appears that the electron withdrawing effect of the geminal dinitro groups is necessary for this nitrolysis to take place. Thus, the reaction of 1-t-butyl-3-hydroxyazetidine (2a) with the nitric acid - acetic anhydride reagent gave 1-t-butyl-3-nitratoazetidine (7a), but no nitrolysis of the t-butyl group took place. Similarly, the 1-i-propyl alcohol gave a high yield of 1-i-propyl-3-nitratoazetidine (7c).



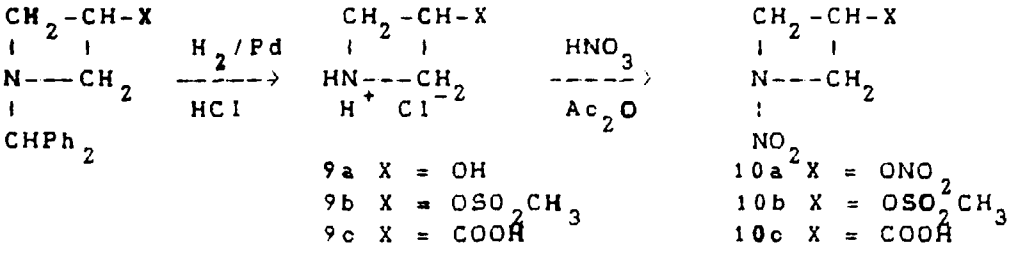
In our synthesis of nitrooxetanes, 3-azidooxetane was reduced to the amine, which was then oxidized to 3-nitrooxetane with peracids[4]. This

approach was examined for the azetidine system. Thus, 1-t-butyl-3-azido-azetidine (8) was prepared in 75% yield by reacting (3a) with sodium azide in methanol. However, when 1-t-Butyl-3-aminoazetidine[11], was then treated with m-chloroperbenzoic acid in refluxing ethylene chloride, no nitro compound was obtained.



A potential method of introducing nitro groups into azetidines that was examined briefly was halogenation of the oximes. 1-t-Butyl-3-oximinoazetidine could not be prepared because of instability of the precursor, 1-t-butyl-3-azetidone.[13] On the other hand, benzhydryl-3-azetidone[13], was obtained from the reaction of the alcohol with oxalyl chloride and dimethyl sulfoxide. This ketone was converted to 1-benzhydryl-3-oximinoazetidine with hydroxylamine. The reaction of N-bromosuccinimide with this oxime cleaved the benzhydryl group to form benzophenone, but no nitro-containing products were isolated. Nitration of this oxime only resulted in deoximation to the ketone.

Another approach to nitroazetidine involved the nitration of azetidines or their salts to form N-nitroazetidines followed by subsequent transformations at the 3- carbon. Hydrogenolysis of 1-benzhydryl-3-hydroxyazetidine with Pearlman's catalyst[9] gave a high yield of of 3-hydroxyazetidinium hydrochloride[14] (9a). Nitration of this salt with nitric acid in acetic anhydride gave an 87% yield of 1-nitro-3-nitratoazetidine (10a).



Nitration of 3-carboxyazetidinium hydrochloride[15,16] (9c) with nitric acid - acetic anhydride gave 3-carboxy-1-nitroazetidine (10c) in 65% yield. Similarly, 3-methanesulfonatoazetidinium hydrochloride[15] (9b) gave 1-nitro-3-(methanesulfanato)azeditine (10b) in 86% yield with this reagent. However, (10b) did not undergo displacement reactions with sodium nitrite or sodium azide. No reaction was observed below 100°C and the nitramine decomposed above that temperature.

Experimental Section

Warning! Nitro azetidines must be considered potentially explosive and treated with caution.

Melting points are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN, and Spang Laboratories, Eagle Harbor, MI. The nmr specta were recorded on a Varian T-60 spectrometer and the chemical shifts are reported in parts per million downfield from tetramethylsilane. Infrared spectra were recorded with a Perkin-Elmer 700 spectrometer.

1-t-Butyl-3-nitroazetidine (5a). A solution of 25 g (0.36 mol) of sodium nitrite in 30 mL of water was added to a solution of 40 g (0.25 mol) of 1-t-butyl-3-(methanesulfonato)azetidine (3a)[11] and 32 g (0.2 mol)

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Trituration of this oil with methylene chloride gave a solid which was recrystallized from ether to give 3.4 g (65%) of (10c), mp 132-134°C: IR (KBr) 3100-2900 (O-H), 1695 (C=O), 1540, 1430 (NO_2) cm^{-1}; NMR (D_2O) & 3.5 (m, 1 H), 4.5 (assym d, J= 3 Hz, 4 H) ppm.

Anal. Calcd for $C_4H_6N_2O_4$: C, 32.88; H, 4.14; N, 19.17. Found: C, 32.85; H, 4.86; N 18.98.

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1. This Work was supported by the Office of Naval Research.

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(0.03 mol) of (9b)[15] was added to a solution of 10.8 mL of 100% nitric acid in 50 mL of acetic anhydride at such a rate that the temperature of the reaction mixture did not exceed 10°C. The solution was stirred for 30 min and poured over 100 g of ice. This mixture was stirred for 2 hrs and the solid which formed was collected. Several recrystallizations from ethanol and chloroform gave 5.25 g (86%) of (10b), mp 75-76°C. IR (CH_2Cl_2) 3050 (C-H), 1530 (NO_2) cm^{-1}. NMR ($CDCl_3$) δ 3.05 (s, 3 H, CH_3-S), 4.6 (m, 4 H, CH_2), 5.1 (m, 1 H) ppm.

Anal. Calcd for $C_4H_8N_2O_5S$: C, 24.36; H 4.09; N, 14.20. Found: C, 24.50; H, 4.22; N, 14.09.

Reaction of (10b) with Sodium Nitrite. A solution of 1.8 g (0.01 mol) of (10b), 0.8 g (0.011 mol) of sodium nitrite, 1.4 g of phlorogluci-nol dihydrate, 0.2 g of urea, and 0.5 g of lithium bromide in 40 mL of DMF was stirred at room temperature for 4 days. NMR analysis showed no reaction, and heating the solution 2 days at 40°C gave 1.55 g (86 %) of recovered (10b).

Reaction of (10b) with Sodium Azide. A solution of 1.8 g (0.01 mol) of (10b) and 1.0 g (0.015 mol) of sodium azide in 30 mL of diethyl-eneglycol was stirred at 80°C for 24 h. NMR and IR analysis showed no reaction. Heating the mixture to 130°C gave an intractable tar.

3-Carboxy-1-nitroazetidine (10c). A solution of 5.0 g (0.036 mol) of (9c)[15] was added to a solution of 10.8 mL of 100% nitric acid in 50 mL of acetic anhydride at a rate such that the temperature of the reaction mixture did not exceed 10°C. The solution was stirred for 8 H at room temperature and was then poured over 200 mL of ice and water. The mixture was extracted with methylene chloride (2 x 100 mL), and then the aqueous layer was concentrated to 25 mL and extracted with ether (3 x 50 mL). The combined ether layers were evaporated in vacuo to give an oil.

solution of 7.0 g (0.055 mol) of oxalyl chloride in 50 mL of methylene chloride at -78°C, and the mixture was stirred for 10 min. Then a solution of 10 g (0.05 mol) of (2b)[8] in 50 mL of methylene chloride was added dropwise and stirring was continued for 30 min. After 22 g (0.11 mol) of triethylamine was added, the solution was warmed to room temperature. The methylene chloride solution was filtered, washed twice with 100 mL portions of water, dried over magnesium sulfate and stripped of solvent to yield a dark oil. This oil was extracted with hot hexane (4 x 50 mL). Evaporation of the hexane gave 6.2 g (60%) of 1-benzhydryl-3-azetidone, mp 94-95°C (methanol), 70-71°C (ethanol), (lit.[13] 77-78).

1-Benzhydryl-3-azetidione was converted to 1-benzhydryl-3-oximino-azetidine with hydroxylamine hydrochloride and sodium carbonate in ethanol: mp 168-169°C (lit.[13] 169-170°C).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.00. Found: C, 75.95; H, 6.28; N, 10.91.

3-Nitrato-1-nitroazetidine (10a). A solution of 10 g (0.1 mol) of (9a)[14] was added to a mixture of 20 mL of 100% nitric acid in 100 mL of acetic anhydride at a rate such that the temperature did not rise above 10°C. The mixture was stirred at room temperature for 6 H and then was poured into 500 mL of ice and water. After 20 min the precipitate which formed was collected and recrystallized from chloroform to give 16.3 g (87%) of (10a), mp 70-71°C, bp 115-118 (0.2 mm), density ($AgNO_3$ solution flotation) 1.61: IR (CH_2Cl_2): 3050 (C-H), 1640 (ONO_2), 1540, 1430 (NO_2) cm^{-1}; NMR ($CDCl_3$) δ 4.5 (m, 4 H, CH_2), 5.3 (m, 1 H, CH) ppm.

Anal. Calcd for $C_3H_5N_3O_5$: C, 22.09; H, 3.09; N, 25.76. Found: C, 22.27; H, 3.06; N, 22.47.

3-Methanesulfonato-1-nitroazetidine (10b). A solution of 5.6 g

1-i-Propyl-3-nitratoazetidine (7c). A solution of 1 ml of concentrated sulfuric acid and 7 mL of 100% nitric acid was cooled to 5°C and 3.0 g (0.02 mol) of 1-i-propyl-3-hydroxyazetidine hydrochloride[8], was added. The solution was stirred for 24 hrs at room temperature and then poured over 100 g of ice. The aqueous solution was neutralized with 10% aqueous potassium hydroxide and extracted with methylene chloride (3 x 50 mL). The methylene chloride solution was dried over magnesium sulfate and solvent was removed to yield 2.8 g (87%) of (7c): IR (CH_2Cl_2) 3000 (C-H) 1620 (-ONO_2) cm^{-1}; NMR (neat) δ 1.0 (d, J=3 Hz, 6 H, CH_3), 2.2 (m, 1 H, $CHMe_2$), 3.0 (m, 2 H), 3.6 (m, 2 H), 5.2 (m, 1 H, ring CH) ppm. This material was analyzed as its hydrochloride, mp 154°C (dec).

Anal. Calcd for $C_6H_{13}N_2O_3Cl$: C, 36.64; H, 6.66; N, 14.24. Found: C, 36.27; H, 6.67; N 14.05.

1-t-Butyl-3-azidoazetidine (8). A solution of 14.0 g (0.049 mol) of 1-t-butyl-3-p-toluenesulfonatoazetidine and 3.5 g of sodium azide in 50 mL of methanol was stirred at room temperature for 18 hrs. Methanol was evaporated and the residue was dissolved in 50 mL of methylene chloride and was washed with 50 mL of water and 50 mL of 10% sodium carbonate solution. The methylene chloride layer was dried over magnesium sulfate and solvent was removed to yield 5.7 g (75%) of crude (8), a light brown oil essentially pure on the basis of NMR. An analytical sample of (8) was obtained by distillation (foaming), bp 50-52 (0.5 mm): IR (CH_2Cl_2) 3000 (C-H), 2140 (-N_3) cm^{-1}; NMR ($CDCl_3$) δ 0.95 (s, 9 H, CH_3), 3.0-4.0 (m, 5 H) ppm.

Anal. Calcd for $C_7H_{14}N_4$: C, 54.52, H, 9.15; N, 36.33. Found: C, 54.66; H, 9.50, N 36.18.

1-Benzhydryl-3-azetidone. A solution of 8.8 g (0.11 mol) of dimethyl sulfoxide in 20 mL of methylene chloride was added dropwise to a

dinitroazetidine was also accomplished with silver nitrate- sodium nitrite in 39% yield and with tetranitromethane in 10% yield. The product was stable for long periods at room temperature.

1,3,3-Trinitroazetidine (1). Acetic anhydride (5 mL) was cooled with an ice bath to 2°C and 1.5 mL of 100% nitric acid was added dropwise. The mixture was stirred for 5 min and 0.75 g (0.0037 mol) of (6a) was added dropwise. A waxy solid precipitated and slowly redissolved. After 1 h, 50 mL of methylene chloride was added, and the solution was washed with 50 mL of water and 50 ml of 10% sodium carbonate solution, and was dried over magnesium sulfate. The solvent was evaporated in vacuo and the residual solid recrystallized three times from carbon tetrachloride to yield 0.25 g (35%) of (1), mp 103-104°C: IR (CH_2Cl_2) 3050 (C-H), 1580, 1420 (NO_2) cm^{-1}; NMR ($CDCl_3$) δ 5.0 (s) ppm; density ($AgNO_3$ solution flotation) 1.83.

Anal. Calcd for $C_3H_4N_4O_6$: C, 18.76; H, 2.10; N, 29.16. Found: C, 18.93; H, 2.16; N 26.81.

1-t-Butyl-3-nitratoazetidine (7a). A solution of 5.0 g (0.038 mol) of 1-t-butyl-3-hydroxyazetidine (2a)[8] in 10 mL glacial acetic acid was added dropwise at 10-15°C to 10 mL of 100% nitric acid and 20 mL of acetic anhydride. The solution was kept at 10°C for 30 min and at 25°C for 5 hrs and was then poured over 100 g of ice. The mixture was neutralized with 10% potassium hydroxide and extracted twice with 50 mL of diethyl ether. The ether solution was dried over sodium sulfate and solvent was removed to yield 3.15 g (47%) of (7a) as a liquid: IR (CH_2Cl_2) 3000 (C-H), 1610 ($-ONO_2$) cm^{-1}; NMR (neat) δ 0.95 (s, 9 H, CH_3), 3.2 (m, 4 H, CH_2), 5.2 (quint, 1 H, CH) ppm. This material decomposed on standing and elemental analysis was not obtained.

1-Benzhydryl-3,3-dinitroazetidine (6b). A solution of 1.0 g (0.0037 mol) of (5b) and 0.30 g (0.0075 mol) of sodium hydroxide in 30 mL of ethanol was stirred for 30 min at room temperature and 1.0 g of sodium nitrite was added. Tetranitromethane (1.0 g, 0.005 mol) was added dropwise with external cooling to keep the reaction mixture under 30°C. After 30 min, the ethanol was evaporated on a rotary evaporator, and 50 mL of water was added. The mixture was extracted with 2 x 50 mL of ether, and the combined ether layers were concentrated to give a waxy solid. Recrystallization from ethanol gave 0.44 g (38%) of (6b), mp 85-86°C: IR (CH_2Cl_2) 3050 (C-H), 1580, 1460 (NO_2) cm^{-1}; NMR ($CDCl_3$) δ 3.95 (s, 4 H, CH_2), 4.4 (s, 1 H, CH), 7.1 (m, 10 H, Ar) ppm.

Anal. Calcd for $C_{16}H_{15}N_3O_4$: C, 61.33; H, 4.80; N, 13.42. Found: C, 61.34; H, 5.06; N, 13.23.

1-t-Butyl-3,3-dinitroazetidine (6a). Freshly distilled (5a) (3.2 g, 0.0202 mol) was dissolved in a solution of 0.84 g (0.021 mol) of sodium hydroxide in 50 mL of water and the solution was cooled to 10°C. Then a chilled solution of 6.9 g (0.1 mol) of sodium nitrite and 1.3 g (0.004 mol) of potassium ferrocyanide in 50 mL of water was added followed by 6.6 g (0.028 mol) of sodium persulfate. The temperature rose to 30°C after 10 min. The mixture was stirred for 1 h and then extracted with methylene chloride (2 x 50 mL). The methylene chloride solution was dried over magnesium sulfate and the solvent removed. The residual liquid was distilled to give 2.44 g (60%) of (6a), bp 70-72°C (0.2 mm), mp 17-18°C: IR (CH_2Cl_2) 3050 (C-H), 1580, 1465 (NO_2) cm^{-1}. NMR ($CDCl_3$) δ 1.0 (s, 9 H, CH_3), 4.0 (s, 4 H, CH_2) ppm.

Anal. Calcd for $C_7H_{13}N_3O_4$: C, 41.38; H, 6.45; N, 20.68. Found: C, 41.66; H, 6.57; N, 20.11.

Oxidative nitration of 1-t-butyl-3-nitroazetidine to 1-t-butyl-3,3-

71.21; H, 6.52; N, 10.10.

Similar results were obtained when (4) was used as the starting material in place of (3b). The reaction did not take place in methanol, and using lithium bromide in place of sodium iodide gave 1-benzhydryl-3-nitroazetidine in smaller yields. The use of anhydrous conditions and the addition of urea to dissolve the sodium nitrite in DMF did not affect the yield.

1-t-Butyl-3-bromoazetidine. A mixture of 29 g (0.1 mol) of (3a), 16 g (0.2 mol) of lithium bromide and 50 mL of acetone was stirred for 24 h at room temperature. The salts were filtered off and the acetone was evaporated on a rotary evaporator. The residual oil was distilled (bp 65-70 ^{o}C at 30 mm) to yield 9.5 g (49%) of 1-t-butyl-3-bromoazetidine; NMR ($CDCl_3$) δ 1.0 (s, 9 H, CH_3), 3.4 (m, 4 H, CH_2), 4.2 (quint, 1 H,) ppm.

Anal. Calcd for $C_7H_{14}NBr$: C, 43.76; H, 7.34; N, 7.29. Found: C, 43.45; H, 7.04; N, 7.19.

1-Benzhydryl-3-iodoazetidine (4). A solution 22 g of (0.66 mol) of of (3b) and 12 g (0.8 mol) of sodium iodide in 100 mL of DMF was stirred at 60 ^{o}C for 5 hrs. The mixture was added to 200 mL of water and extracted with ether (3 x 100 mL). The combined ether layers were stripped of solvent in vacuo to give a dark brown oil, which was dissolved in 30 mL of methylene chloride and was passed through 10 g of silica gel. Evaporation of the methylene chloride gave a waxy solid which was recrystallized from ethanol to give 16.3 g (70%) of (4), mp 96-97 ^{o}C. NMR ($CDCl_3$) δ 3.6 (m, 4 H, CH_2), 4.2 (m, 1 H), 4.4 (s, 1 H), 7.0 (m, 10 H, Ar) ppm.

Anal. Calcd for $C_{16}H_{16}NI$: C, 55.02; H, 4.62, N, 4.00. Found: C, 55.29; H, 4.80; N, 4.03.

of phloroglucinol dihydrate in 300 mL of methanol, and the reaction mixture was allowed to stand at 0°C for 48 hrs. The resulting brown solution was stripped of solvent in vacuo at 30°C and 200 mL of water was added. This unstable mixture was extracted rapidly with methylene chloride (3 x 100 mL), and the combined methylene chloride solutions were dried over magnesium sulfate and solvent was removed. The resultant oil was distilled to yield 2.5 g (8%) of 1-t-butyl-3-nitroazetidine (5a), bp 50-52°C (0.1 mm). IR (CH_2Cl_2) 3000 (C-H), 1550, 1430 cm^{-1} (NO_2); NMR ($CDCl_3$) δ 0.95 (s, 9 H, CH_3), 3.55 (asym d, J=3 Hz, 4 H, CH_2), 4.90 (quint, J=3 Hz, 1 H) ppm.

Anal. Calcd for $C_7H_{14}N_2O_2$: C, 53.14; H, 8.72; N, 17.70. Found: C, 52.87; H, 8.66; N, 16.33.

Warning: On occasion, compound (5a) decomposed violently during distillation. The compound was stable at -15°C for long periods, but at room temperature in a sealed tube it decomposed in several days.

1-Benzhydryl-3-nitroazetidine (5b). A solution of 31.5 g (0.1 mol) of 1-benzhydryl-3-(methanesulfonato)azetidine (3b)[11], 7.5 g (0.11 mol) of sodium nitrite, 12 g (0.075 mol) of phloroglucinol dihydrate, 14 g (0.1 mol) of sodium iodide, and 20 mL of water in 200 mL of DMF was stirred at 50°C for 48 hrs and was then added to 150 mL of water. The mixture was extracted with ether (3 x 100 mL), and the solvent was removed in vacuo to give 14.1 g of oil, shown by NMR analysis to be a 1:1 mixture of 1-benzhydryl-3-iodoazetidine (4) and (5b). Column chromatography (silica gel, methylene chloride) of this oil yielded 3.0 g (11%) of 1-benzhydryl-3-nitroazetidine, mp 135-136°C. IR (CH_2Cl_2) 3050 (C-H), 1550, 1440 (NO_2) cm^{-1}; NMR ($CDCl_3$) δ 3.5 (asym d, J=3 Hz, 4 H, CH_2), 4.3 (s, 1 H, CH), 4.8 (m, 1 H, CH), 7.0 (m, 10 H, Ar) ppm.

Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C,

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